

# Reduced Birthweight and Length in the Offspring of Females Exposed to PCDFs, PCP, and Lindane

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The objective of this study was to investigate a broad range of adverse health outcomes and their potential association to wood preservative used in daycare centers. This article focuses on reproductive effects. A sample of 221 exposed teachers was provided by the employer's liability insurers. A comparison group ( $n = 189$ ) insured by the same two organizations was recruited from nonexposed daycare centers. In a face-to-face interview, job history and reproductive history of 398 female teachers were ascertained. Data on exposure were provided, including measurements on concentration of pentachlorophenol (PCP) and lindane in wood panels, and of PCP, lindane, polychlorinated dibenzo-*p*-dioxins and dibenzofurans in indoor air. An exposure matrix based on individual job history, independent exposure information from each center, and reproductive history was set up with regard to the vulnerable time windows for each pregnancy. Using this approach, 49 exposed and 507 nonexposed pregnancies were identified, including 32 exposed and 386 nonexposed live births. For subgroup analyses the observations were restricted to independent pregnancies, excluding multiple and consecutive births. The data were analyzed with linear regression techniques, taking confounders into account. The crude median difference between exposed and nonexposed was 175 g in birthweight and 2 cm in length. Controlling for confounders, the results show a significantly reduced birthweight ( $p = 0.04$ ) and length ( $p = 0.02$ ) in exposed pregnancies, even after restricting the data to independent pregnancies and pregnancies for which data could be validated from the mother's health cards. These differences were not explained by differences in gestational age, indicating that a toxic effect, which could cause small-for-date newborns, might have affected the fetus. **Key words:** birth length, birthweight, fetotoxic effects, lindane, PCDDs, PCDFs, pentachlorophenol, wood preservatives. *Environ Health Perspect* 103:1120–1125 (1995)

Wood preservatives were extensively used in former western Germany. Not only was exterior wood treated for preservation, but paneling and other interior wood structures were treated, an especially popular practice in the 1960s. Wood preservative preparations contained pentachlorophenol (PCP) and  $\gamma$ -hexachlorocyclohexane (HCH) as biocidal substances. Wood preservatives were also contaminated with trace amounts of polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDDs, PCDFs), which were formed during production processes. These compounds have the potential to volatilize and become entrained in ambient air or dust particles, thus becoming available for human contact. PCDDs and PCDFs have been found in indoor air of exposed daycare centers at picogram per meter levels, with higher chlorinated congeners such as hexa-, hepta-, and octachlorodibenzo-*p*-dioxins and furans (HxCDD, HxCDF, HpCDD, HpCDF, OCDD, OCDF) as major contaminants (1).

No epidemiological study regarding reproductive effects of mixed exposure to PCP, HCH, and PCDDs and PCDFs is available so far. In a case study, 22 of 90 women with histories of multiple spontaneous abortions, unexplained infertility,

menstrual disorders, or early onset of menopause were found to have elevated blood levels of PCP ( $>25 \mu\text{g/l}$ ) and/or HCH ( $>100 \mu\text{g/l}$ ) (2). In women with fertility problems, chlorinated hydrocarbons such as HCH were found in higher concentrations in follicular fluid and cervical mucus from women who remained infertile compared to women who ultimately conceived (3).

Regarding human exposure to PCDDs, PCDFs, and related compounds during pregnancy, only a few studies are available so far. A study on reproductive effects due to the contamination of soil with PCDDs and PCDFs in eastern Missouri ( $n = 386$  exposed,  $n = 772$  nonexposed) identified a nonsignificantly increased risk ratio of 1.5 for low birthweight ( $<2500 \text{ g}$ ) and an average reduction of 20 g for the offspring of mothers living in the vicinity of the exposed areas (4). Decreased birthweights were reported for pregnancies in Taiwanese women who consumed rice oil contaminated with large amounts of polychlorinated biphenyls and PCDFs (5,6). The difference in birthweights between eight exposed and eight nonexposed pregnancies was about 510 g. In an Austrian study on health effects in the vicinity of a copper recovery plant releasing heavy metals and

PCDD/PCDF pollution, a reduction of birthweight, length, and head circumference was detected (7). However, only the latter achieved statistical significance in the crude analysis presented.

A reduction in birthweight has been demonstrated for HCH in mice (8). Embryoletality (9–12) and decreased fetal or gestational weight gain (9,13) were reported in rats and/or hamsters exposed to PCP.

Thus, whether chronic, low-level exposure causes adverse effects on human reproduction is controversial. Our hypothesis was that indoor exposure to a mixture of PCP, HCH, and PCDDs/PCDFs reduces birthweight and birth length in the offspring of mothers exposed during pregnancy.

## Methods

In a cross-sectional investigation in 1987–1988, exposed employees insured under the employer's liability scheme, working in daycare centers treated with wood preservatives in the State of Hamburg and its vicinity, were invited to participate in the study. The control group, also insured under the same scheme, was directly recruited from untreated daycare centers, each of which was located close to one of the exposed daycare centers. Of those identified as exposed under the employer's liability scheme, 68% participated in the study; 62% of the workforce in daycare centers not treated with wood preservatives participated.

The study population consisted of 410 daycare workers (men and women), 210 with known exposure and 200 without. In the course of the investigation, 12 employees from the nonexposed group were found to have been exposed at a former daycare center. One of the persons with employer's liability insurance had not experienced occupational exposure to wood preservatives. Thus, the exposed group consisted of 221 persons and the nonexposed group of 189.

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Two hundred fourteen of the exposed group and 184 of the control group were women. They contributed 556 pregnancies with an individual maximum of 5 pregnancies.

A broad range of adverse health outcomes was investigated. Medical checkups with blood sampling and 24-hr urine samples and face-to-face interviews inquiring about occupational and reproductive history were undertaken. We asked the women to bring their official medical record documents (mother's health card) to validate data on gestational age, pregnancy outcome, birthweight, and length. Informed consent was obtained for all data collection procedures. Female medical students who had undergone interview training conducted the interviews.

In addition, individual occupational history and lifestyle exposure were ascertained: occupational conditions (six time periods), smoking (three periods of active smoking, four periods of nonsmoking), alcohol consumption (three periods of higher consumption), exposure to wood preservatives in private or weekend homes (three or five periods, respectively, subject's information supported by product and brand names). For each pregnancy, information on the outcome and its date, gestational age, parity, complications, desire for a child (woman/partner), malformations, and birthweight and length was requested, providing a full reproductive history of up to five pregnancies for all women. Age of the mother at conception and parity were computed using these data.

Measurements from the wood paneling and of the indoor air were conducted independently of this study. In 1986 the Federal State of Hamburg initiated a screening program to detect wood preservative exposure in all daycare centers in Hamburg. In facilities with a PCP concentration in the wood exceeding 100 ppm, indoor air measurements were conducted, or, if only few wood panels existed (area in  $\text{m}^2/\text{indoor volume in m}^3 < 0.2$ ), the paneling was removed (14). No such program existed outside Hamburg. However, communities and church-owned daycare centers on the border of Hamburg also followed this approach. In our sample, PCP concentrations in the wood >100 ppm had been measured in 24 facilities. The control group was working in 35 nonexposed facilities. Not all indoor air measurements were complete for all three components (PCP, HCH, and PCDDs, and PCDFs). In the exposed group the median concentration of PCDDs/PCDFs in toxic equivalency factors for 2,3,7,8-TCDD (TEFs), used by the Federal Health Office in Germany, was

0.5  $\text{pg}/\text{m}^3$ . The PCP concentration was about 0.25  $\mu\text{g}/\text{m}^3$ , and HCH was about 0.2  $\mu\text{g}/\text{m}^3$  (median). The PCDD/PCDF indoor concentration and the PCP concentration in wood were correlated (Spearman  $r = 0.48$ ,  $n = 19$ ,  $p = 0.039$ ), but not indoor PCDD/PCDF and HCH in the wood paneling (Spearman  $r = -0.31$ ,  $n = 13$ ,  $p = 0.28$ ). However, to avoid assumptions about indoor air pollution, a facility was defined in this study as exposed when the wood paneling showed PCP concentrations higher than 100 ppm.

For single pregnancies, exposure to wood preservatives was checked for each time window (uncertainty  $\pm 1$  month). A pregnancy was defined as being exposed if the employee worked in any of the 24 exposed facilities at any time during her pregnancy.

In a similar way, the values of potential confounders were addressed. Active smoking, alcohol consumption, and exposure to wood preservatives in private homes was checked according to personal history data for each time window of the pregnancy ( $\pm 1$  month). All pregnancies before or after such risk periods were defined as nonexposed with regard to wood preservatives or the potential confounders. Although some indoor air measurements were available for most occupational facilities, exposure to wood preservatives in daycare centers and in private homes was dichotomized (exposure versus nonexposure). Extrapolation from the measurements in 1986 and 1987, consideration of the duration of exposure in the respective time window (either in months or in weekly working hours), or their combination was assumed to provide less valid information.

For women who smoked during pregnancy, the months of smoking, not the number of cigarettes, were taken into account because the reported number was thought to be less reliable due to social pressures against smoking. For active smokers, the period of smoking in relation to gestational age was computed. The "usual" amount of alcohol consumed was determined by using the frequency of consumption (daily, three to four times a week, one to two times a week, about once a month, never) and the amount of wine/beer or liquor consumed (0.02–0.5 l) and its respective concentration of alcohol. This same amount was used for past alcohol consumption. For periods in which a woman said she drank more, the amount was doubled.

Age of the mother, parity, and gestational age (according to the mother's health card or comparable documents) were controlled for in the analyses. The increase in weight during pregnancy is not linear. The squared

values of gestational age show a more appropriate relation and were taken into consideration when evaluating birthweight.

Exposure effects were adjusted for height and weight of the mothers. For both variables measurements taken during 1987–1988 were used, since no information was available on these measurements before pregnancy.

The analyses were conducted using SAS software (SAS Institute, Cary, North Carolina) and included descriptive information and results of multiple regression analyses on birthweight and birth length (15,16). The multivariate normal distribution of the two outcome variables in models, including all predictors, their homoscedasticity, and collinearity of the predictors, was checked.

The 556 observations (pregnancies) contributed by 398 are not independent. Thus, a subgroup including the first exposed pregnancy for women who had at least one exposed pregnancy and the first pregnancy for women who only had unexposed pregnancies, excluding twins, was also analyzed. To take occupational status also into account, regression analyses were conducted in six groups: 1) the total group of observations excluding twins; two outliers in the distribution of birthweights (>6200 g) had to be eliminated to achieve a multivariate normal distribution and one outlier in birth length smaller than 34 cm had to be eliminated; 2) a subgroup in which the weight and length could be validated according to official medical documents (mother's health card); 3) a subgroup consisting of all pregnancies during which the mother was employed for at least 1 month of the pregnancy; 4) a subgroup based on the total group with restriction to first exposed and first nonexposed pregnancy; 5) a subgroup formed by including only those pregnancies of group 2 and group 4; 6) a subgroup formed by including only those pregnancies of group 3 and group 4.

The final model, with all confounders that do not disturb the exposure–weight or exposure–length relation eliminated (17), is presented for the total group (group 1). Regarding the results of the other subgroups, only the exposure effects controlling for all other confounders are presented.

The two outliers in the analysis of birthweights and the one outlier in birth lengths were excluded for statistical reasons only (no normal distribution of the residuals). Other than the fact that these birthweights (>6200 g) could not be validated from the mother's health card, there is no medical justification to exclude these two outliers (see Fig. 2). Thus, the analysis was repeated including these outliers with a

correction by transforming weights according to Blom (18). The newborn with the birth length of 27 cm (see Fig. 2), however, came from a 22-year-old mother with a severe atopic skin disease, who was under treatment during pregnancy. Thus we did not include this case in the analysis.

## Results

Overall, only 49 of 556 pregnancies occurred in the time window of occupational exposure to wood preservatives (Table 1). Thirty-two exposed and 386 nonexposed pregnancies were carried to full term and resulted in live birth. Restrictions on single first exposed and first unexposed pregnancies reduced the number of exposed pregnancies to 32. Of these, only 27 were first-exposed live births (Table 1). Exposed pregnancies ended more often as induced abortions, spontaneous abortions, or as cesarean sections (Table 1).

Two births with twins (2 of 32, 6.3%) led to a higher prevalence of twins in the exposed pregnancies than in the nonexposed. Complications during pregnancies were more frequent in the nonexposed group. Validation of pregnancy data according to medical documents (mother's health card) was possible in more than 80% of exposed and only in about 50% of nonexposed pregnancies (Table 1). This fact is explained by the introduction of the mother's health card in 1969–1970 and its coincidence with popular use of wood preservatives after 1970.

Table 2 shows the rank and outcome of exposed pregnancies which resulted in live births. The 32 live births originated from 29 women. Three women each had two exposed live births. Nine women had both exposed and nonexposed children. Of these, the single first exposed or first nonexposed was taken into consideration for the subgroup of independent observations.

Birthweights were reduced by about 150 g in exposed pregnancies taking all observations into account, as well as those restricted to the first exposed pregnancies and the pregnancies for which data could be validated from the mother's health card (Table 3). In exposed pregnancies, the babies were also shorter (50 cm in comparison to 52 cm in nonexposed; Table 3). Figure 1 shows that the reduction in birthweights cannot be attributed to single outliers, but is due to a general shift in the distribution of the weights. From Figure 2, it is obvious that weight and length co-scatter. Only one observation (length of 27 cm) seems to be outlying.

Potential confounders were not equally distributed among exposed and nonex-

**Table 1.** Outcome of pregnancies of women exposed to wood preservatives and of women not exposed: all and first pregnancies

Outcome	All exposed (n = 49)	All nonexposed (n = 507)	First exposed (n = 32)	First nonexposed (n = 256)
Induced abortion (%)	20.4	14.4	25.0	14.8
Miscarriage (%)	14.3	8.7	18.8	7.0
Stillbirth (%)	0	0.8	0	0.8
Cesarean section (%)	14.3	5.7	12.5	6.3
Regular birth (%)	51.0	70.4	43.8	71.1
	Last two outcomes, exposed (n = 32)	Last two outcomes, nonexposed (n = 386) <sup>a</sup>	First exposed with live births (n = 27)	First nonexposed with live birth (n = 231)
Complications during pregnancy (%)	15.6	20.8	14.8	21.7
Twins (%)	6.3	1.0	0	0
Gender: male <sup>b</sup>	46.9	50.0	48.2	49.4
Verified with mother's health card (%)	87.5	50.3	85.2	53.7

<sup>a</sup>Includes four pregnancies for which data on birthweight and length are missing.

<sup>b</sup>Gender data are missing for 0.8% of all nonexposed pregnancies and for 0.4% of first nonexposed pregnancies.

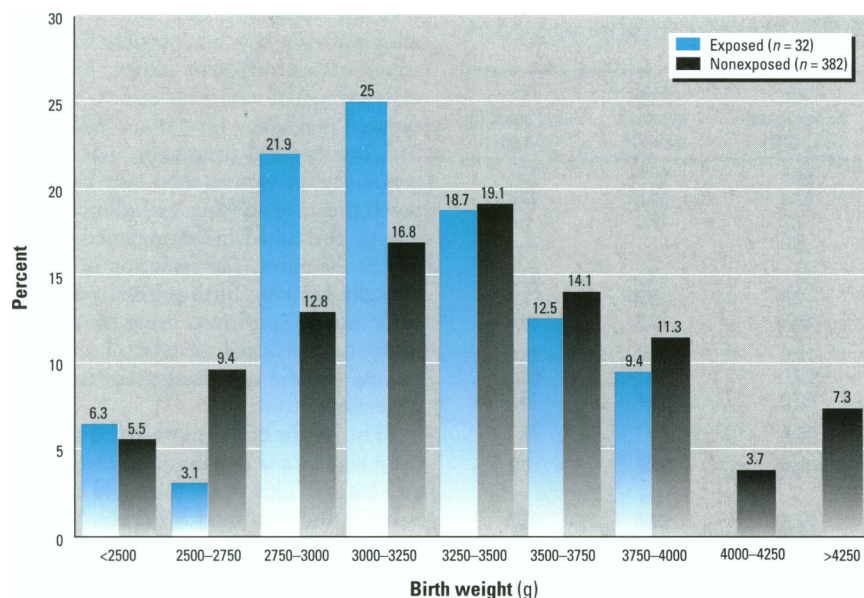
**Table 2.** Exposed pregnancies with outcome and rank

No. of exposed live births	Frequency	Pregnancy rank					Exposure during pregnancy to wood preservatives				
		1	2	3	4	5	1	2	3	4	5
1	1	IA	IA	LB			No	Yes	Yes		
1	1	IA	IA	Twins			No	Yes	Yes		
1	1	IA	IA	LB	SA		Yes	Yes	Yes	No	
1	1	IA	CS				No	Yes			
1	1	IA	LB				No	Yes			
1	1	SB	SA	SA	CS	IA	No	Yes	No	Yes	No
1	1	SA	LB	LB	LB	IA	No	Yes	No	No	Yes
1	2	CS					Yes				
1	1	CS (twins)					Yes				
1	1	CS	SA	SA	LB		No	No	Yes	Yes	
1	1	CS	SA	CS	CS		No	Yes	Yes	No	
1	8	LB					Yes				
1	1	LB	IA				Yes	No			
1	1	LB	SA	SA	LB		No	Yes	Yes	Yes	
1	1	LB	SA	LB			No	Yes	Yes		
1	1	LB	LB				No	Yes			
1	1	LB	LB				Yes	No			
1	1	LB	LB	LB			No	No	Yes		
2	1	IA	LB	IA	LB		Yes	Yes	Yes	Yes	
2	1	IA	LB	CS	LB		No	No	Yes	Yes	
2	1	LB	LB				Yes	Yes			

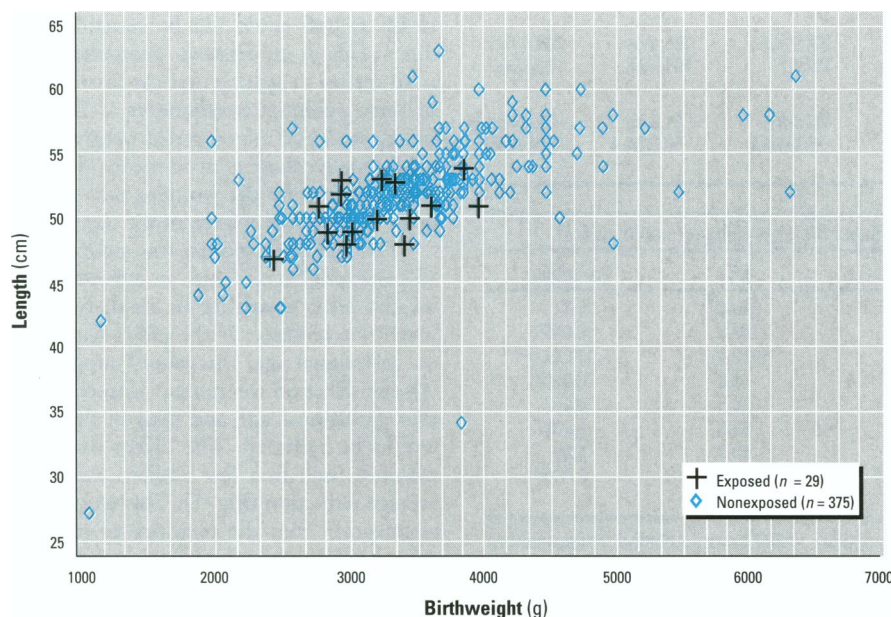
Abbreviations: IA, induced abortion; SA, spontaneous abortion; LB, live birth; CS, cesarean section.

**Table 3.** Median and 5th and 95th percentiles of birthweight and birth length for offspring of women exposed to wood preservatives and of women not exposed, with and without verification by the mother's health card

Outcome		All exposed	All nonexposed	First exposed	First nonexposed
Without verification					
Birthweight (g)	n	32	382	27	230
	Median	3175	3350	3200	3345
	5th/95th	2430/3910	2400/4500	2780/3910	2450/4500
Birth length (cm)	n	31	379	26	229
	Median	50	52	50.5	52
	5th/95th	47/53	47/57	48/53	47/57
With verification					
Birthweight (g)	n	28	192	23	123
	Median	3115	3350	3060	3370
	5th/95th	2430/3870	2570/4200	2780/3740	2570/4150
Birth length (cm)	n	50	52	50.0	52
	5th/95th	47/53	47/56	48/53	48/56



**Figure 1.** Birthweights for exposed and nonexposed pregnancies. Numbers above bars are actual percentages.



**Figure 2.** Scatterplot of birthweight and size, exposed and nonexposed pregnancies. Spearman rank correlation of weight and length: nonexposed,  $r = 0.70$ ,  $p = 0.001$ ; exposed,  $r = 0.52$ ,  $p = 0.004$ .

posed pregnancies (Table 4). Women who were exposed during pregnancy tended to be older and to have a higher parity. There were only minor differences for smoking during pregnancy and for alcohol consumption. All exposed pregnancies occurred in employed women. Exposure to wood preservatives in private homes occurred more frequently for exposed pregnancies. Also, the desire for a child was more prevalent in exposed pregnancies.

For the group including all observations with live births, we estimate that a given exposed birth could have been on

average 217 g heavier if it had not been exposed, controlling for necessary confounders (Table 5). The effect was even stronger when the analysis was restricted to observations which were validated by the mother's health card (-259 g; Table 6) or to observations which presented the first exposed or nonexposed pregnancies (-303 g; Table 6). The association is weaker and does not gain statistical significance in the subgroup of women who were employed during pregnancy when two outliers are included ( $p = 0.078$ ).

The birth length of exposed children

was statistically significantly reduced in exposed pregnancies (-1.34 cm, Table 7). This reduction is of nearly equal length in all subgroups (Table 7). However, the effect does not gain statistical significance in three of the five subgroups.

## Discussion

Recruitment of the exposed group was based on information provided by the employer's liability insurers. The control group, also insured under the same scheme, had to be approached in a different way. To reduce potential differences, we asked nonexposed daycare centers in the vicinity of the exposed facilities to participate. The proportion of participation was lower in the reference group (62%) compared to the exposed group (68%). However, there are no hints of selection biases with regard to educational level, smoking, and total number of children (data not displayed). Also a restriction to pregnancies of female teachers of the exposed daycare centers did not change the results (birthweight: -272.5 g,  $p = 0.02$ ,  $n = 224$ ; birth length: -1.37 cm,  $p = 0.039$ ,  $n = 221$ ).

The sampling of the daycare centers and the ascertainment of indoor exposure was performed without knowledge of birthweights and lengths. Birthweights and lengths, however, were ascertained with some knowledge of the exposure and could therefore be biased. Birth data such as weight, length, gestational age, complication during pregnancy, and sex of child was, for the majority of observations (85% of the exposed, 54% of the nonexposed; Table 1), validated from medical notes documented in the mother's health card. In the subgroup with validated information, the results are not dependent on the recall of the mother. This subgroup includes only pregnancies which occurred between 1969 and 1987. The findings did not change when the analysis was restricted to this subgroup (Table 7).

Recall, however, might affect the information on smoking and alcohol consumption. Nevertheless, there is no reason to suspect that a misclassification of these confounders is related to exposure (Table 4).

The reduction in birth length compared to birthweight is less impressive in the five subgroups (Table 7). However, it should be borne in mind that the measurement of the length of a newborn is more dependent on individual techniques than weight is. Consequently, measurement errors are more likely with birth length, and thus the chance of detecting an effect for this outcome is smaller.

In the total group, the effect of exposure could be due to few exposed mothers

**Table 4.** Distribution of potential confounders (percentages) in births for mothers exposed to wood preservatives and nonexposed (excluding twins)

Confounder		All exposed pregnancies (n = 32)	All nonexposed (n = 382)	First exposed (n = 27)	First nonexposed (n = 231)
Age at conception (years)	<25	25.0	56.5	29.6	70.6
	25–35	59.4	42.2	59.3	28.6
	>35	15.6	1.1	11.1	0.4
	Unknown		0.3		0.4
Smoking during pregnancy	No	65.6	69.1	63.0	67.1
	≤3 months	12.5	2.6	14.8	2.6
	>3 months	21.9	28.3	22.2	30.3
Consumption of alcoholic beverages	No	12.5	14.9	11.1	12.6
	≤12 g/day	71.9	64.9	74.1	68.0
	>12 g/day	15.6	20.2	14.8	19.5
Employed		100	63.4	100	72.7
Wood preservatives in private homes		21.9	5.0	22.2	6.1
Desire for a child	Woman	93.8	87.6 (1 unknown)	92.6	85.3 (1 unknown)
	Partner	87.5	87.6 (9 unknown)	88.9	86.2 (4 unknown)
Parity: nullipara		65.6	59.2	70.4	97.6
Gestational age	Median	9.2 months	9.2 months	9.2 months	9.2 months
	5th/95th percentile	8.3/9.4	8.3/9.7	8.7/9.4	8.3/9.7
Height of mother	Median	166.4 cm	164.1 cm	166.4 cm	164.4 cm
	5th/95th percentile	157/184	151/177	157/184	151/176
Weight of the mother at examination	Median	66.2 kg	61.4 kg	61.9 kg	65.9 kg
	5th/95th percentile	51.5/85.7	50.0/84.4	50.0/84.4	50.5/85.0

**Table 5.** Effect of the exposure of wood preservatives on birthweight, controlling for confounders<sup>a</sup>

Predictors	Parameter estimates	SE	Probability
Intercept	127.7	340.3	0.71
Exposure to wood preservatives in daycare centers (with two outliers included)	-217.1 (-230.3)	105.8 (119.4)	0.0409 (0.0423) <sup>b</sup>
Gestational age * gestational age (months <sup>2</sup> )	33.1	3.6	0.0001
Age at conception (years)	10.6	6.3	0.092
Gender of the child ( <i>f</i> = 1, <i>m</i> = 2)	180.1	52.5	0.0007
Complications during pregnancy	-61.4	66.3	0.36
Explained variance: R <sup>2</sup> = 21.5	<i>F</i> -value: 21.66	df = 5	0.0001
Probability of a normal distribution of the residual: 0.25			

<sup>a</sup>*n* = 402, *n* = 10 missing variables in some predictors, two outliers >6200 g are excluded, except where indicated.

<sup>b</sup>Based on Blom-transformed values to achieve a multivariate normal distribution:  $y_i = \Psi(r_i - 3/8)/(n + 1/4)$ , with  $\Psi$  = inverse cumulative normal (Probit) function,  $r_i$  = rank, and *n* = number of nonmissing observations (18).

**Table 6.** Comparison of the effects of wood preservatives on birthweight and length in the five subgroups controlling for all potential confounders

Subgroup	<i>n</i>	Birthweight			<i>n</i>	Birth length		
		Parameter estimate	SE	Probability		Parameter Estimate	SE	Probability
Data validated from mother's health card <sup>a</sup>	216	-259.2	104.8	0.0142	215	-1.22	0.54	0.0242
Women employed during pregnancy (with two outliers included)	265 (267)	-220.2 -191.6	110.2 123.3	0.0468 (0.078) <sup>b</sup>	263	-1.12	0.65	0.0865
First exposed or nonexposed pregnancy (with two outliers included)	253 (255)	-303.2 (-286.7)	119.2 (134.2)	0.0142 (0.018) <sup>b</sup>	252	-1.34	0.67	0.0477
Data validated from mother's health card <sup>a</sup>	145	-317.0	121.2	0.0099	144	-1.09	0.61	0.0764
Woman employed during pregnancy (with two outliers included)	187 (189)	-310.9 (-277.2)	126.5 (148.0)	0.015 (0.031) <sup>b</sup>	187	-1.44	0.75	0.0542

<sup>a</sup>The weights of the two outliers were not confirmed in the mother's health card.

<sup>b</sup>Based on Blom-transformed values in order to achieve a multivariate normal distribution:  $y_i = \Psi(r_i - 3/8)/(n + 1/4)$ , with  $\Psi$  = inverse cumulative normal (Probit) function,  $r_i$  = rank, and *n* = number of nonmissing observations (18).

with more than one baby. Due to the small sample size, it was not possible to analyze strata with a different parity. However, restricting the observations to the first exposed pregnancy for women who had at least one exposed pregnancy, and the first pregnancy for women who only had unexposed pregnancies (thus excluding an effect due to correlated measurements) did not reduce the effect. The inclusion of two statistically outlying birthweights, which also could not be confirmed using the mother's health card, reduced the effect in three subgroups, but did not change the results substantially.

The height of the mother was a statistically significant predictor of birthweight and length. This predictor could be eliminated in the final models (Tables 5 and 6). Height of the mother is, however, included in the comparisons in Table 7. An effect could also be seen for the woman's weight, which was ascertained at the examination, not before the pregnancy. Thus, this variable is only a substitute. Height and weight of the fathers could not be controlled for due to lack of information. However, there is no reason to assume that the distribution of these potential confounders is different in exposed and nonexposed pregnancies. Additionally, there is no evidence that diseases suffered by the women, such as diabetes mellitus, are related to the exposure.

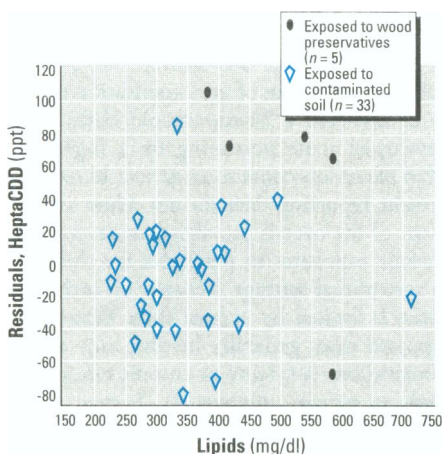
The effect of exposure was independent of gestational age. Thus, an adverse effect on the fetus resulting in small-for-date newborns is likely. If the effect depended on gestational age, this would support an adverse effect on the mother in such a way that gestational age and thus birthweight would be reduced. The effect does not manifest itself in a few outliers, but in an average reduction (Fig. 1). This stresses the assumption that the majority of exposed pregnancies were affected, not just a few sensitive ones.

One limitation of this study is the absence of an indicator of the body burden,

**Table 7.** Effect of the exposure of wood preservatives on birth length controlling for confounders<sup>a</sup>

Predictors	Parameter estimates	SE	Probability
Intercept	32.14	3.37	0.0001
Exposure to wood preservatives in daycare centers	-1.34	0.35	0.0201
Gestational age (months)	2.02	0.35	0.001
Age of the mother (years)	0.03	0.03	0.31
Gender of the child ( $f = 1, m = 2$ )	0.79	0.28	0.0052
Smoking during pregnancy (proportion of gestational age)	-0.49	0.33	0.14
Alcohol consumption during pregnancy	-0.34	0.24	0.15
Complications during pregnancy	-0.66	0.36	0.0643
Explained variance: $R^2 = 12.2\%$	$F$ -value: 7.86	$df = 7$	0.0001
Probability of a normal distribution of the residual: 0.19			

<sup>a</sup> $n = 401$ ,  $n = 8$  have missing variables in some predictors, one outlier <34 cm is ignored.



**Figure 3.** Residuals of the blood concentration of heptaCDD per lipid basis (ppt) not explained by age and the Abdel-Malek Index (22). Residuals = actual values – predicted values; predicted heptaCDD = age \* 2.15 - Abel-Malek Index \* 0.10; Abel-Malek Index =  $f_s * 10^6 * (\text{weight})^{1.2} * (\text{height})^{3.3}$ ;  $f_s = 3$  for women, 4 for man (14); lipids = sum of cholesterol and triglycerides. Explained variance:  $R^2 = 33.1\%$ .

since no individual measurements of PCDDs/PCDFs, PCP, or HCH during or after pregnancy are available. One reason for this is that the pregnancies took place before exposure and potential health effect had been determined. However, measurements of PCP in children from daycare centers exposed to wood preservative before and after removing the wood paneling show a clear reduction of PCP in urine samples from about 17  $\mu\text{g/l}$  to 4  $\mu\text{g/l}$  (19). Additionally, few measurements of PCDD/PCDF in fat samples exist from persons exposed to wood preservatives. The comparison of five findings, which were ascertained by ERGO Forschungsgesellschaft in Hamburg with 33 measurements in an adult group exposed to contaminated soil (20) ascertained by the same laboratory, does not reveal a significant increase in TEFs (21) but significantly higher values for heptaCDD, a

congener which is typical for wood preservatives (Fig. 3). Thus, these additional findings support the assumption that indoor exposure could have increased the body burden of PCP and PCDDs/PCDFs.

The detrimental effect, however, cannot be attributed to one single group of substances but to three groups: PCP, HCH, or PCDDs/PCDFs. Our findings of an adverse effect seem to confirm previous findings on these compounds (12–13). In summary, the results of this study stress the need for future investigation of the effects of wood preservatives and of PCDDs and PCDFs on the development of the fetus, as reduced birthweight is a childhood risk factor for a range of adverse health effects.

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